and Mail
BOX AF

AE
1600

BOX AF
RESPONSE AFTER FINAL REJECTION
EXPEDITED PROCEDURE
EXAMINING GROUP
PATENT

Customer No. 22,852
Attorney Docket No. 03806.0532

#11
JCL
3/19/03

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of:	
Chin-Wen CHI et al.	Group Art Unit: 1614
Application No.: 10/083,565	Examiner: J. GOLDBERG
Filed: February 27, 2002	
For: USE OF DOCETAXEL FOR TREATING HEPATOCELLULAR CARCINOMA	

Commissioner for Patents
Washington, DC 20231

REQUEST FOR RECONSIDERATION AFTER FINAL REJECTION

Sir:

In response to the Final Office Action mailed January 9, 2003, Applicants respectfully request reconsideration and withdrawal of the rejections set forth in that Office Action in view of the following remarks and those of the previous responses. In addition, Applicants request that the Office specifically respond to both their previous remarks and the following remarks. Applicants make this request so that the positions of both Applicants and the Office are clear, which will facilitate review on appeal. Claims 7-9 and 12-22 are pending in this application, claims 13-15 having been withdrawn by the Office as directed to non-elected inventions.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

I. *Restriction Requirement*

In the Final Office Action, the Office maintains the Restriction Requirement, and withdraws claims 13-15 from consideration. (Final Office Action at page 2.) Applicants respectfully submit that non-elected claims 13-15 are directed to the same invention as elected claims 7-9, 12, and 16-22. More specifically, claims 13-15 merely recite specific embodiments of the method claimed in claim 7. Thus, the claims are directed to the same subject matter, and should all be examined in this application. For at least this reason, the Restriction Requirement is improper, and should be withdrawn.

II. *Rejection Under 35 U.S.C. § 103*

In the Final Office Action, the Office maintains the rejection of claims 7-9, 12, and 16-22 under 35 U.S.C. § 103(a) as unpatentable over Broder *et al.* (Final Office Action at pages 2-3.) In particular, the Office states that Applicants' remarks in the Amendment filed October 15, 2002, were unpersuasive because Broder *et al.* states that "oral paclitaxel, docetaxel, other taxones and their prodrugs and derivatives" can be used to treat hepatocellular carcinoma. (Final Office Action at page 3.) Applicants respectfully submit that this point was raised by the Office in the first Office Action (dated July 30, 2002; page 3), in which the Office asserted that, although Broder *et al.* did not disclose intravenous use of docetaxel, such use would have been obvious to one of ordinary skill in the art. Applicants traverse this rejection, reassert the arguments presented in the Amendment of October 15, 2002, and request that the Office reconsider those arguments along with the following arguments.

Applicants respectfully submit that Broder *et al.* 1) fails to motivate one of ordinary skill in the art to intravenously administer docetaxel to a patient in an amount sufficient to treat a hepatocellular carcinoma, and 2) fails to provide a reasonable expectation of success in treating a

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

hepatocellular carcinoma with intravenous administration of docetaxel. Applicants also submit that Broder *et al.* fails to motivate one to achieve the doses specifically recited in claims 17-19 and 22, and fails to provide a reasonable expectation that such doses would be suitable for intravenous administration of docetaxel.

First, Broder *et al.* fails to motivate one of ordinary skill in the art to intravenously administer docetaxel to a patient in an amount sufficient to treat a hepatocellular carcinoma. As discussed previously, Broder *et al.* is directed to improving the oral bioavailability of pharmaceutical agents that are poorly absorbed in the gastrointestinal tract, such as paclitaxel and docetaxel. See Broder *et al.* at col. 1, lines 21-25, for example. Broder *et al.* does not disclose or suggest treating hepatocellular carcinoma by intravenous administration of docetaxel. The closest Broder *et al.* comes to such a disclosure is found in Figures 30 and 31, and the accompanying text at col. 8, lines 11-24.[1] These portions of Broder *et al.* disclose experiments designed to monitor the levels of docetaxel in the blood system of rats treated, by intravenous and oral routes, with 1) docetaxel and 2) docetaxel with cyclosporin. It is important to recognize that the experiments are designed to monitor the levels of docetaxel in the blood, not to treat hepatocellular carcinoma. Indeed, there is no disclosure whatsoever in Broder *et al.* of levels of docetaxel in the liver, much less a disclosure of any activity of docetaxel, administered intravenously or orally, on hepatocellular carcinoma. Rather, the only intravenous administration of docetaxel by Broder *et al.* is performed solely to provide a benchmark (*i.e.*, a

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

[1] Applicants note that the Office has identified a passage bridging col. 15, lines 32-44, as relevant to the present method claims. Applicants submit that the passage identified by the Office is not as relevant to the passage discussed herein because the passage cited by the Office is directed to oral administration only.

positive control) for the presence of docetaxel in the blood system. Oral administration is performed solely to determine if the docetaxel can be absorbed into the blood system.

Thus, at the most, Broder *et al.* provides a motivation to orally treat a hepatocellular carcinoma. However, it provides no motivation whatsoever to treat, or even attempt to treat, a hepatocellular carcinoma by intravenous administration of docetaxel, alone or with another agent.

This point was raised in the Amendment of October 15, 2002. However, the Office did not respond to it in the Final Office Action of January 9, 2003. In fact, to this point in prosecution, the Office has provided no reason why one of ordinary skill in the art would have been motivated to intravenously administer docetaxel to a patient in an amount sufficient to treat hepatocellular carcinoma. Applicants request that the Office address this point and clearly provide a reason why one would be motivated by Broder *et al.* to intravenously administer docetaxel to a patient in an amount sufficient to treat hepatocellular carcinoma. In the absence of such a motivation, Applicants submit that the presently claimed invention is not rendered obvious by Broder *et al.*

Second, even if one were to find that Broder *et al.* provides a motivation to intravenously treat hepatocellular carcinoma with docetaxel, Broder *et al.* fails to provide a reasonable expectation of success in doing so. The only data presented by Broder *et al.* that could be considered relevant to treatment of hepatocellular carcinoma is data showing that paclitaxel can be found in the liver after it is administered to a subject. However, this does not show that the paclitaxel is present in an amount sufficient to treat hepatocellular carcinoma (*i.e.*, in an effective amount). Furthermore, it does not show that an effective amount of paclitaxel can be localized to the liver. Finally, and most importantly, this data does not show, or even suggest, that docetaxel can be administered to a patient in an amount sufficient to treat hepatocellular carcinoma.

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

This point was raised in the Amendment of October 15, 2002. However, the Office did not address it in the Final Office Action of January 9, 2003. Applicants request that the Office address this point now, and provide a reason why the disclosure that paclitaxel can be found in the liver after administration would provide a reasonable expectation that one could successfully intravenously administer docetaxel in an amount sufficient to treat hepatocellular carcinoma. In the absence of such a reasonable expectation, Applicants submit that the presently claimed invention is not rendered obvious by Broder *et al.*

Third, Broder *et al.* fails to motivate one to achieve the doses specifically recited in claims 17-19 and 22, and fails to provide a reasonable expectation that such doses would be suitable for intravenous administration of docetaxel. More specifically, claims 17-19 and 22 recite defined doses. In the Office Action of July 30, 2002, the Office implied that there would be a reasonable expectation that the same amounts of docetaxel administered orally would be effective intravenously. In response, Applicants presented reasons why the Office's apparent position was erroneous. In summary, Applicants argued that that the doses for oral administration of a drug are significantly different than the doses for intravenous administration, and that disclosure of one dose does not render the other obvious.

The Office has not yet responded to Applicants' argument. Applicants request that the Office address this point now, and provide a reason why one would have had a reasonable expectation of successfully using the oral doses disclosed for paclitaxel for intravenous administration of docetaxel. In the absence of such a reasonable expectation, Applicants submit that the presently claimed invention of claims 17-19 and 22 is not rendered obvious by Broder *et al.*

In summary, Applicants submit that Broder *et al.* fails to render the presently claimed invention obvious. Accordingly, Applicants request that the Office reconsider and withdraw the

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com

rejection of claims 7-9, 12, and 16-22 under 35 U.S.C. § 103(a) as unpatentable over Broder *et al.* If, after considering the comments presented by Applicants in the Amendment of October 15, 2002, and the present Request, the Office maintains that one or more of claims 7-9, 12, and 16-22 are obvious over Broder *et al.*, Applicants request that the Office specifically discuss why Applicants' arguments have been found not persuasive.

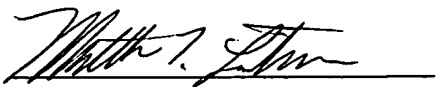
III. *Conclusion*

Applicants respectfully submit that this application is in condition for allowance. Therefore, Applicants respectfully request that the Office reconsider and withdraw the outstanding rejections, rejoin claims 13-15 with claims 7-9 and 12-22, and permit this application to issue as a U.S. patent in due course. If the Office believes anything further is necessary in order to place this application in even better condition for allowance, Applicants respectfully request that their undersigned representative be contacted at the telephone number or e-mail address listed below.

Please grant any extensions of time required to enter this Request, and charge any required fees to our Deposit Account No. 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW, GARRETT & DUNNER, L.L.P.

By: 

Matthew T. Latimer
Reg. No. 44,204
571-203-2714
matthew.latimer@finnegan.com

Date: March 14, 2003

FINNEGAN
HENDERSON
FARABOW
GARRETT &
DUNNER LLP

1300 I Street, NW
Washington, DC 20005
202.408.4000
Fax 202.408.4400
www.finnegan.com